Chronic Pain: The Good, The Bad, and The Ugly

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Focus on the Good
Improve Awareness of the Bad and Ugly

- The Good = Therapeutic options to treat pain
- The Bad = Don’t always work
- The Ugly = Opiate abuse/addiction
Introduction and Overview

▪ The good
  • Chronic pain is a complex topic and a common problem seen in underwriting
    o We have methods to identify and treat chronic pain
      • Overview of types of chronic pain
      • Treatment Modalities
        o Pharmacologic vs nonpharmacologic

▪ The bad
  • Treatments don’t work in the majority of cases
  • Limited data to guide treatment
  • Co-morbid conditions are an obstacle to effective treatment
Introduction and Overview

- The **ugly** is prescription drug use/abuse in the U.S. today
  - Opiate use for chronic pain
    - Recognizing aberrant use of narcotics
      - Overuse / addiction
      - Polypharmacy
        - Substances of abuse: MJ, stimulants, sedatives
  
- Mortality issues
  - Overdose
Goals

Present an approach to underwriting and risk classification

- Define pain and review therapeutic options for treatment
- Comorbid conditions that make treatment difficult
- Distinguish acceptable and appropriate use of these substances from at-risk use or abuse, dependence and addiction
- Develop a rational approach to analysis of risk based on type of pain, treatment, and comorbid conditions
  - Insurable vs uninsurable
Acute versus Chronic Pain

- **Acute pain** is immediate pain, and a warning signal the body receives that damage had been done or is imminent
  - **Acute pain** is finite, and usually has an identified cause and a time-limited course
    - Post operative pain, trauma related pain

- **Chronic pain** is the result of temporary or permanent changes in and around the peripheral and central nervous systems
  - **Chronic pain** is pain that extends beyond the expected period of healing
    - Common time intervals used: 3 months to 6 months depending on the source

What Causes Pain Physiologically?

- Chronic pain can be multifactorial

- 2 Major types of pain based on pain receptor type
  - Chronic nociceptive pain is caused by ongoing tissue injury that continuously stimulates a type of nerve called a nociceptor
    - Superficial pain is initiated by activation of nociceptors in skin or superficial tissues
    - Deep somatic pain is initiated by stimulation in ligaments, tendons, bones, blood vessels, fascia and muscles, and is dull, aching or poorly localized
    - Visceral pain originates in the organs: appendicitis, cholecystitis, pleurisy

Neuropathic Pain

- Neuropathic pain commonly relates to diabetes, nerve compression or arthritis and degenerative disease
  - Neuropathic pain is due to a dysfunction in the nervous system
    - Peripheral pain originates in the peripheral nervous system
    - Central pain originates in the brain or spinal cord
- Diabetic neuropathy is the most common neuropathy in the western world!
  - It is a function of disease duration as well as disease control
  - Risk of painful neuropathy is increased in type II diabetics, and women
  - 50% of diabetics will eventually develop neuropathy

Classification of Chronic Pain

- **Inflammatory pain**: arthritis and infections

- **Mechanical or compressive pain**: kidney stone, visceral pain from compression of expanding mass
  - Injury that stimulates pain receptors (nociceptors) in the skin, bones, or joints

- **Neuropathic pain**
  - CNS abnormalities or **central pain** (neuropathic): multiple sclerosis, post stroke pain
  - **Peripheral pain** (neuropathic): diabetic neuropathy, post-herpetic neuralgia

- **Musculoskeletal pain**: back pain, fibromyalgia
  - Chronic pain in muscles and fascia: back pain, fibromyalgia
  - Trigger points may be present

Types of Chronic Pain

- Musculoskeletal: 41%
- Neuropathic: 30%
- Other: 29%
Prevalence of Chronic Pain

- 116 million Americans suffer with chronic pain
  - 12% of all Rxs are written for pain

- Women > men

- 80% back pain

- Seniors

- Socioeconomic
  - Greater disability related to work
  - Access and utilize more health care services

- Other health conditions
Changes in Prescribing Patterns

Editorial in New England Journal of Medicine

- Previously, opioids were not indicated in the long-term treatment of chronic pain

- This philosophy changed drastically in the late 1990s and into 2000
  - New pain management guidelines from the Joint Commission for the Accreditation of Healthcare Organizations (JCAHO) in 2000
  - In 2001 California mandated all licensed physicians (except radiologists and pathologists) take a full-day course on “pain management”
  - The self-report of pain was to be treated above any other considerations

- Patient satisfaction surveys and Internet physician ratings became powerful determinants of a physician’s payment and business

- Addiction counseling and treatment is time-consuming, poorly reimbursed and often unavailable, while treatment with opiates is profitable and pain clinics are ubiquitous
Medical Challenges Related to Diagnosis of Chronic Pain

- There is no way to prove someone’s claim of pain is true or false!
- Diagnosis can be difficult – especially in identifying the source of the chronic pain
- No tests are sufficiently sensitive or specific for a diagnosis
  - MRI/ Radiologic appearance may not correlate well with nature or location of pain
  - Electromyography (EMG) and Nerve conduction studies (NCS) used for peripheral neuropathy may not be helpful in polyneuropathies with predominant small fiber involvement

Comorbidities

High portion associated with psychiatric comorbidity

- Chronic pain is associated with higher rates of depression and anxiety as well as insomnia and other sleep disturbances caused by the pain or the medications
  - Post traumatic stress disorder
  - Substance abuse
- Forgetfulness, difficulty with attention and difficulty completing tasks may be present
- Decreased physical activity, possibly due to fear of exacerbating the pain
- Limited ability to perform ADLs or IADLs
Comorbidities

- Depression & Anxiety
- Opioid Abuse
- Decreased Physical Activity
- Cognitive Impairment
When To Refer to Pain Specialist?

- Recommendation statement from the American Academy of Pain Medicine:
  - Current treatment is not helping, or the pain interferes with daily function,
  - If the primary care provider begins to feel uncomfortable continuing the current treatment with the patient
  - To confirm or establish the diagnosis and offer suggestions on management

- “Chronic pain like all chronic medical illness requires patient self-management. Cure is rare and complete pain relief is rarer. Patients do best when they adopt a new lifestyle not solely dictated by pain.”

Non-Pharmacologic Treatments

Combinations of modalities may have beneficial effect long term

- Requires practice and consistency
- Physical therapy/training= Stretching to develop ROM and muscle conditioning
- Biofeedback = used to treat migraine and tension type headaches
  - Some improvement in headache frequency and medication consumption
- Nerve stimulation= can consist of local stimulation vs spinal cord stimulation
  - Variable degrees of success with the local stimulators AKA Transcutaneous electrical stimulation or TENs unit
  - Deep brain stimulation for intractable severe, persistent pain states has shown some success in experienced hands
- Acupuncture = Heavy component of placebo effect , superior outcomes in many studies
  - May be effective for certain types of pain in certain types of people

Pharmacologic Treatments

- **Analgesics**
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Opiates

- **Adjuvant Medications**
  - Antidepressants
    - TCAs and SNRIs
  - Muscle relaxers
  - Anticonvulsants (gabapentin, pregabalin)
  - Corticosteroids
  - Nerve block injections
  - Topical analgesic agents
Pharmacologic Approach to Chronic Pain

- Currently available treatment modalities on average result in only about 30% decrease in pain
  - Multimodality approach works best
    - Use medications in conjunction with other modalities not as sole treatment

- Nonopioid analgesics - work best for nociceptive pain
  - ASA, Tylenol, NSAIDs
    - Toxicities exclude use in certain individuals
      - Liver toxicity in doses above 4 GM/day of Tylenol
      - Renal toxicity with NSAIDs in elderly individuals with renal insufficiency
NSAIDs

- NSAIDs have been shown to be associated with a higher risk of coronary artery disease and stroke
  - “Selective” COX -2 inhibitors (Vioxx, Celebrex) vs. “non-selective”
  - All have some risk
    - Vioxx > Celebrex
    - ibuprofen > naproxen
  - Risk with short-term as well as long-term use
  - Most significant with history of multiple other risk factors

Pharmacologic Approach to Chronic Pain

- Antidepressants to treat chronic pain
  - Tricyclic antidepressants (TCA)
    - Most commonly used: amitriptyline, doxepine, imipramine, desipramine
  - Serotonin norephinephrine reuptake inhibitors (SNRIs)
    - Duloxetine (Cymbalta) used for fibromyalgia

  - Both classes of drugs have been shown to be effective in neuropathic pain
  - Mechanism of action is not understood well
  - TCAs have multiple side effects – not always well tolerated

Pharmacologic Approach to Chronic Pain

- Anticonvulsants used in chronic pain therapy
  - This class of drugs used for pain control since the 1960s
    - Approved by the FDA for the treatment of neuropathic pain
      - Gabapentin (Neurontin) - post herpetic neuralgia
      - Pregabalin (Lyrica) – post herpetic neuralgia and diabetic neuropathy
      - Carbamazepine (Tegretol) used for trigeminal neuralgia

The Bad …

Less than 50% response to initial therapy

- “Combination therapy is often required, because less than half of patients with neuropathic pain will respond to a single agent. However, evidence is scant regarding the efficacy and safety of combination treatment.”

- “In a 2013 Cochrane review of 31 trials of opioids for neuropathic pain, there was equivocal evidence of efficacy after short-term (less than 24 hours) opioid treatment; intermediate (less than 12 weeks) treatment was effective (33 percent pain relief in 57 percent of patients compared with 34 percent with placebo), but risk of bias in the studies was high.”


Prescription Opioid Abuse
Introduction

- Austin Box was a linebacker for the University of Oklahoma football team
- He was a starter and considered a pro prospect
- He suffered a number of injuries during his career but continued to play through many of these
- On May 19, 2011, at the age of 22, he collapsed at a friend’s house and later died
- According to a report in USA Today, his autopsy revealed the presence of oxymorphone, morphine, hydrocodone, hydromorphone and oxycodone as well as alprazolam, an anxiolytic
- The cause of death was said to be pulmonary edema and aspiration pneumonia from mixed drug toxicity
What is an opiate?

- Is a subclass of opioid that occur naturally in the opium poppy plant
  - Act in the brain and peripheral nervous system on receptor sites to produce analgesia, potential euphoria, and most importantly from our vantage point Respiratory Depression
  - Morphine - Heroin is a derivative of morphine and the most abused opioid used intravenously (IV)
    - Crosses the blood brain barrier in a matter of seconds
  - Codeine

- Synthetic opioids: Fentanyl and Methadone
- Semisynthetic opioids: Oxycodone and Hydrocodone
- All have tremendous addictive potential!
Medications

Morphine (MS Contin)
Hydromorphone (Dilaudid, Exalgo)
Oxycodone (Percodan, Oxycontin)
Fentanyl (Duragesic)
Hydrocodone (Vicodin, Lortab, Norco)
Oxymorphone (Opana)
Levorphenol
Codeine
Pentazocine (Talwin)
Propoxyphene (Darvon)
Meperidine (Demerol)
Tramadol (Ultram)
Tapentadol (Nucynta)
Treatment Effects

The ugly side of the story

- The current prevalence of substance abuse disorders in patients taking long-term opioids is high
- **Drug addiction** is a condition in which there is a compulsive use of a substance that causes dysfunction and continued use despite that dysfunction
- **Pseudoaddiction** is medication-seeking behavior by patients whose pain is undertreated
  - It differs from addiction in that adequate dosing results in improved function
  - This concept is very controversial and has not been scientifically validated
- **Tolerance** is a pharmacological state of requiring increasing amounts of a drug to achieve a desired response
- **Physical dependence** is a pharmacologic property of a drug and does not necessarily relate to or occur with addiction
The Ugly Truth

- Drug addiction/pseudoaddiction
- Treatment Effects
  - Physical dependence
  - Tolerance
  - Overdose (accidental or intentional)
Overdose Death Rates 2002-2015
Increasing incidence of overdoses
- Graph derived from National Institute for Health Statistics demonstrates a 2.2X increase in deaths related to overdose during 2002-2015
  - Increase in the use of illicit drugs
  - Drug use is increasing in the individuals aged 50-60 possibly due to aging baby boomers

Increasing incidence of deaths associated with prescription opioid use
- Associated with 14,800 deaths in the U.S. in 2008; rate quadrupled since 1999
  - Exceeds the deaths due to heroin and cocaine combined
Substance Abuse

After alcohol, marijuana has highest rates of dependence
CDC Guidelines for Prescribing Opioids

Published 2016

- Major Guidelines Developed- Summarized Below
  - Develop goals and treatment plan to treat chronic pain: nonopioid medications should be the first choice if medications are required
  - No long acting opioids for acute pain and recommend lowest effective dose possible
    - Guidelines are to use lower dose and avoid titrating medication above 90 MME
    - Re-evaluate the response to medication within 1-4 weeks (avoid using narcotics for over 3 months if possible)
  - Avoid the concurrent use of narcotics and benzodiazepines if possible
    - Use urine drug screens to insure compliance and eliminate polysubstance abuse
Risk Factors For Overdose and Misuse

- High average daily dose
  - Use the MME calculator to determine if high dose
- Multiple prescribers
- Prolonged use
- Use of long acting agents
- Concurrent use of benzodiazepines

Morphine Milligram Equivalent (MME)

- All medication potencies are based on morphine as the standard for comparison
  - There are calculators on the internet: website:

- Risk for overdose increases substantially as the MME increases
  - RR of overdose in individuals taking 20 to < 50 MME is between 1.3- 1.9
  - RR of overdose in individuals taking 50 to < 100 MME is between 1.9- 4.6
  - RR of overdose in individuals taking >100 MME is between 2.0 – 8.9

CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016
MMWR. March 18, 2016/ 65(1); 1-49.
Medications

- **Methadone (Dolophine)**
  - Previously used in treatment of narcotic addiction rather than for pain relief
  - Now is more frequently being used in chronic pain settings
    - Relatively poor choice for this given variable pharmacodynamics due to active metabolic byproducts: can cause QT prolongation on EKG, cardiac arrhythmias, overdose potential
    - Many state and other formularies require it in these settings due to its low cost despite a significantly increased incidence of overdoses
    - Regardless of the indication for which it is being used, it suggests a higher-risk situation

- **Opioid agonist/antagonists**
  - These are used in treatment of addiction though also are used in pain treatment
  - Buprenorphine (Butrans), Butorphenol, Naloxone, Naltrexone
  - Suboxone (buprenorphine/naloxone) is used primarily for the treatment of opiate addiction and its use requires special surveillance
What about Cannabis and Cannabinoids?

- Use of these drugs for chronic pain is controversial
  - The data to support use of these substances is ongoing and conflicted
  - There are more than 60 types of cannabinoids derived from the cannabis plant
    - THC (tetrahydrocannabinol) has psychoactive properties and is manufactured in the US
      - Indicated for the treatment of nausea and vomiting induced by chemotherapy as well as appetite stimulation in wasting diseases
    - Dronabinol (Marinol)
    - Nabilone (Cesamet)
    - Nabiximois (Salivex) – not approved in the USA- approved in Canada to treat spasticity due to MS
      - Spray that is absorbed into the oral mucosa
What about Cannabis and Cannabinoids?

- **What does the research tell us?**
  - It does show some merit as a pain reliever vs placebo in some trials
    - NO cancer related pain trials have been performed
  - Vaporized and or smoked seems to benefit some individuals with neuropathic pain

- **What is the current philosophy ?**
  - Clinical use of cannabinoids for cancer pain should be limited to the drugs that are currently on the market despite the fact they are not indicated for cancer pain
    - Reasonable to try cannabinoid if patient is refractory to opioids or other adjuvant analgesics
    - Many concerns: potency, titrate dose, drug to drug interactions
  - The use of THC is illegal at the federal level


Approach to Underwriting

- MVR
- Financials
- APS
  - Indications
  - Stability of dose if chronic
  - Use of other sedating substances (i.e., alcohol, marijuana)
  - Pain contracts
  - Use of pain specialists or pain clinics (+/-)
    - Little evidence this improves outcomes
  - Recognize the dilemma doctors face in treating pain adequately yet avoiding long-term problems
Approach to underwriting

- Prescription data
  - Number of refills (risk increases as number of refills increases)
  - Number of different narcotics prescribed
  - As-needed vs. scheduled vs. both (combination of both is highest risk)
  - Other types of psychoactive or sedating medications (i.e. muscle relaxers, sleeping pills, anxiolytics, antidepressants, medical marijuana)
  - Multiple prescribers
  - Increased risk in those with OSA
Approach to Underwriting

- Distinguish appropriate from inappropriate use
  - Duration of use: short term vs long term use
  - Multiple doctors/prescriptions
  - Forged or altered prescriptions
  - Applicant wants more pills than doctor is willing to prescribe
  - Applicant “loses” prescription
  - Applicant uses other people’s meds
  - Criticism
  - Past history of alcohol or drug abuse
  - Pain management specialist or pain contracts
Approach to Underwriting

- Red flags
  - Multiple driving infractions
  - Accidental injuries
  - Young males
  - Affluent, high-profile
  - Erratic behavior/deterioration in work or school performance
  - Arrhythmias
  - Multiple prescribers
  - Multiple other psychoactive and/or sedating medications
    - History of Use of Methadone or Suboxone
Approach to Underwriting

Points for concern when underwriting

• “Allergies” to numerous analgesics other than the drug of choice
• Financial problems
• Hepatitis
• Route of administration other than oral (e.g., patch, IM, IV, prn)
Ratings

- Short-term or episodic (as-needed or prn) use without criticism or inappropriate use can generally be rated quite favorably
- Chronic use with stable doses and no criticism or inappropriate use can also be rated favorably
- Current chronic use with criticism, inappropriate use or other red flags is usually highly rated to decline
- Caution is warranted in individuals with a history of depression even if the depression is not ratable
Ratings

- Cross-addiction
  - Other drugs
  - Alcohol
  - Very high risk/decline

- Recovery
  - Generally long-term recovery is not achieved without an initial in-patient treatment regimen followed by continued counseling and support group attendance like Narcotics Anonymous
  - Generally long postpone period before consideration is possible
Summary

- Drug abuse is an ever-increasing problem encountered by underwriters, with significant mortality implications.
- Distinguishing appropriate and inappropriate use is the key to underwriting these individuals.
- A number of factors identify inappropriate and high-risk use, and these cases are generally rated or declined.
- Recovery is possible, but postpone periods are required before we can reconsider.
Questions?
Thank you for your attention.